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AMENDED

APPLICATION FOR A STANDARD PATENT OR A STANDARD PATTENT OF ADDITION

6

I/We TERUMO KABUSHIKI KAISHA

of 44-1, 2-chome, Hatagava, SShibuya-ku, Tokyo, Japan

(54) hereby apply for the grant of a ☑ standard patent ☐ patent of addition for an invention entitled

MEDICAL INSTRUMENT

558588

which is described in the accompanying ☐ provisional ☑ complete specification.

(72) The actual inventor(s) of the said invention is/are AKIRA TAKAHASHI, MASAHIRO NUDESHIMA, KYUTA SAGAE, HIROSHI HOSHINO, HIROSHI SUZUKI and YUKO KOMAKURA

(74) My/our address for service is SANDERCOCK, SMITH & BEADLE, 207 Riversdale Road, (P.O. Box 410) Hawthorn, Victoria, 3122 Attorney Code SA

(ONLY TO BE USED IN THE CASE OF A CONVENTION APPLICATION)

Details of basic application (s) –

NUMBER	COUNTRY	DATE OF APPLICATION	ISO Code

APPLICATION ACCEPTED AND AMENDMENTS
5.12.86

Dated this 11th day of June 19 86

TERUMO KABUSHIKI KAISHA

(Signature)

SANDERCOCK, SMITH & BEADLE

TO

THE COMMISSIONER OF PATENTS

This form must be accompanied by either a provisional specification (Form 9 and true copy) or by a complete specification (Form 10 and true copy)

PATENTS ACT 1952

PATENT DDECLARATION FORM
(CONVENTIONN OR NON-CONVENTION)

DECLARATION IN SUPPODRT OF APPLICATION FOR A PATENT

Insert name of applicant.

In support of the application made by Terummo Kabushiki Kaisha trading as TERUMO CORPORATION

Insert title of invention.

for a patent for an invention entitled: "MEDDICAL INSTRUMENT"

Insert full name(s) and address(es) of person(s) making declaration. If applicant a company person must be authorised to make declaration.

I/We Mitsuc TOZAWA of 44-1, 2-c-chome, Hatagaya, Shibuya-ku, Tokyo, Japan

do solemnly and sincerely declare as follows:s:

* 1. (a) ~~I/WE am/are the applicant(s) for the patent.~~
* OR (b) I am authorized by the al abovementioned applicant to make this declaration on its behalf.

* 2. (a) ~~I/WE are the actual inventor(s) of the invention.~~
* OR (b) Akira TAKAHASHI of f 6-3,Funakubo,Fujinomiya-shi,Shizuoka-ken, Japan; Masahiro NUDESHIMA of 3 379-1,Nakajima-cho, Fujinomiya-shi, Shizuoka-ken,Japan; Kyuta SAGAAE of 5-2-9,Fujimidai,Fuji-shi,Shizuoka-ken,Japan;Hiroshi HOSHINO of 1 1-10-1310,Wakabadai,Asahi-ku,Yokohama-shi, Japan;Hiroshi SUZUKI of 540 Waasedatsurumaki-cho,Shinjuku-ku,Tokyo,Japan and Yuko KOMAKURA of 406-1,Minnowa-cho,Kohcku-ku,Yokohama-shi,Japan

Delete alternatives which do not apply

Insert name(s) and address(es) of actual inventor(s).

I/We are the actual inventor(s) of the inventioron and the facts upon which the applicant(s) is/are entitled to make the application are as follows:—

Insert details of entitlement to apply, e.g. Applicant is assignee of inventor(s)

The said applicant is the assiignee of said inventors

Delete 3 and 4 if application non-convention. Otherwise insert details of basic application(s).

3. The basic application(s) as defined by Section 141 of the Act was/were made in the following country or countries on the following date(s) by the following applicant(s)

in _____ on _____ 19__
by _____
in _____ on _____ 19__
by _____
in _____ on _____ 19__
by _____
in _____ on _____ 19__
by _____

4. The basic application(s) referred to in paragraph 3 of this Declaration was/were the first application(s) made in a Convention country in respect of the invention the subject of the application.

Place and date of Signature.

Declared at Tokyo, Japan this 17th day of January 19 86

NO ATTESTATION
OR SEAL

Terumo Kabushiki Kaisha trading as ~~TERUMO CORPORATION~~

Signature(s) of declarant(s).

Mitsuo TOZAWA, President

To: The Commissioner of Patents, Australia

SANDERCOCK, SMITH & BEADLE,

P.O. Box 410, Hawthorn, 3122, Australia
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(54) ANTIMICROBIAL TREATED MEDICAL DEVICES

(71) TERUMO KABUSHIKI KAISHA

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(72) AKIRA TAKAHASHI, MASAHIRO NUDESHIMA, KYUTA SAGAE, HIROSHI HOSHINO, HIROSHI SUZUKI AND YUKO KOMAKURA

(74) SA

(57) Claim

1. A medical instrument having a fluid path or container wherein the instrument ccomprises:

a main body of the medical insstrument; and

at least one antimicrobial aggent located on at least a surface of the fluid path of the maain body and selected from the group consisting of N-(fluorrodichloromethylthio)-phthalimide, 2-(4-thiazolyl)-benzimmidazole, N,N-dimethyl-N'-phenyl-(N-fluorodichloromethylthiio)-sulphamide, 2,4,5,6-tetrachloroisophtharonitrile, paracchlorometaxylenol, sodium 2-pyridinethiol-1-oxide, zinc 2-pyrridinethiol-1-oxide, and 2,4,4'-trichloro-2'hydroxyphenyl ethher, wherein the agent is at an effective level such tthat the increase of microorganisms contacting the surfaoce is suppressed.

558588

COMMONWEALTH OF AUSTRALIA

Form 10

PATENTS ACT 1952-1969

COMPLETE SPECIFICATION

(ORIGINAL)

FOR OFFICE USE

Class Int. Class

Application Number: 52834/86

Lodged:

Complete Specification—Lodged:

Accepted:

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This document contains the amendments made under Section 49 and is correct for printing.

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Melbourne

TO BE COMPLETED BY APPLICANT

Name of Applicant: TERUMO ~~CORPORATION~~ KABUSHIKI KAISHA

PATENT OFFICE AUSTRALIA 16(3)

Address of Applicant: 44-1,2-chome, Hataggaya, Shibuya-ku, Tokyo, Japan.

Actual Inventor: Akira Takahashi, Maasahiro Nudeshima, Kyuta Sagae, Hiroshi Hoshino, Hiiroshi Suzuki, Yuko Komakura.

Address for Service: 207 Riversdale Roadd, Hawthorn, 3122, Victoria, Australiaa.

Complete Specification for the invention entitled: MEDICAL INSTRUMENT

The following statement is a full description of this inventioion, including the best method of performing it known to me:—

Background of the Invention

1. Field of the Inventioon

The present inventioon relates to a medical instrument which can prevvent bacterial contamination in fluids.

2. Description of the Prrior Art

Fluid circuit devicees such as respiratory and urinary circuit devices mmust often be connected to patients in a surgical orr post-surgical ICU or CCU control system.

The lifetime of thesse circuit devices has increased along with the developmennt of patient monitoring systems and advances and improvemeents in medical equipment in recent years.

Howeyer, most patienbts requiring such fluid circuit devices have a low reesistance to infection. Non-pathogenetic bacteria for healthy bodies may become pathogenetic or cause proliferation of pathogenic bacteria leading to bacterrial exchange for patients with a low resistance to iinfection, thus resulting in infection.

Medical instruments ssuch as fluid circuit devices are often used at high temmperatures and humidities. These conditions are very suitable for proliferation of molds and present major faactors contributing to infection in medical instrumentts, especially circulatory

of time.

These medical instrumeents are normally used in a sterilized state. When micsroorganisms such as bacteria exist in a fluid contained in such a medical instrument or flowing therethrough, thne same problem as described above is encountered.

Different problems are inherent in individual medical instruments. Contanmination countermeasures for portions directly contactinqg fluids in the instruments have been proposed for each individual instrument.

For example, in additicon to general contamination factors described above, a respiratory circuit device is also subjected to contamhination by expired air since the device has an open circculating path. Furthermore, artificial respiration bypasses the upper trachea, and the infection resistance inhherent to the trachea is lost.

In order to prevent contamination, the circuit in question is sterilized, disiinfected or cleaned. In addition, (1) the circuit iss frequently replaced with a new one: (2) a bacteria filtter is used: or (3) a built-in heater circuit is used tco decrease the amount of water contained in the circcuit.

However, in case (1), aa large number of circuits for replacement are requireod, increasing maintenance expenses and resulting in ann impractical application.

In case (2), the bacterria filters do not have

uniform quality. In addition,, contamination caused by expired air cannot be preventeed.

In case (3), it is possibble to delay a contamination time in the circuit, bbut circuit handling is complex in procedure.

As another example, a cloosed urinary guide bag is not easily contaminated witth bacteria. However, contamination of the bag with bacteria does occur for various reasons. Once thee urine passageway is contaminated, the closed effecct of the bag is lost. Although antibiotics are systeemically administered to the patient,. bacteria reappearr in the urine due to the proliferation of resistant baccteria.

In order to prevent the cblosed urinary guide bag from infection, (1) the bacterria entered in the bag must not be allowed to flow in the reverse direction; or (2) these bacteria must be completeely killed.

In technique (1), an intravenous drip infusion chamber is arranged at the inleet port of the bag to block the reverse flow path of bacteria. However, infection cannot be completely prevented with this technique.

In technique (2), formalinne (conventionally) or hydrogen peroxide (in recent ddevelopments) is added in the bag to provide resistance tto bacteria. However, once the urine held in the bag is removed, such resistance is lost. Therefore, cumbersome replacement of

a. sterilizer is required. When the urine flows in the reverse direction, the sterillizer may enter the patient's body.

U.S. Patent 4,515,593 ddiscloses a baloon catheter having a certain antimicrobiall agent on its surface.

Summary of thhe Invention

It is an object of the prresent invention to provide a medical instrument which is safe for patients and which provides continuous and efffective prevention against bacteria and microorganism conttamination.

The above object of thae present invention can be achieved by the present inventiion to be described below.

A medical instrument having a fluid path or container wherein the instrument comprisees:

a main body of the medicall instrument; and

at least one antimicrobiall agent located on at least a surface of the fluid path of thae main body and selected from the group consisting of N-((fluorodichloromethylthio)-phthalimide, 2-(4-thiazolyl)-beenzimidazole, N,N-dimethyl-N'-phenyl-(N-fluorodichloromethyylthio)-sulphamide, 2,4,5,6-tetrachloroisophtharonitrile, pparachlorometaxylenol, sodium 2-pyridinethiol-1-oxide, zinc 2-pyridinethiol-1-oxide, and 2,4,4'-trichloro-2'hydroxyphenyll ether, wherein the agent is at an effective level suech that the increase of microorganisms contacting the suurface is suppressed.

Brief Description cof the Drawings

Figure 1 is a front view sshowing an embodiment of the present invention;

Figure 2 is a partially cuttaway front view of the

medical instrument shown in Fig. 1;

Fig. 3 is a sectional view showing another embodiment of the present invention; and

Fig. 4 is a sectional view for explaining a test for measuring an effect of the present invention.

Detailed Description of the Preferred Embodiments

A medical instrument of the present invention has a fluid path and/or container which contains a gas (e.g., expired gas, inspired gas, and anesthetic gas) and/or a liquid (e.g., urine, a fluid therapy liquid, and an infusion solution). A predetermined compound is present on at least a surface of the flow path and/or container which contacts the fluid.

According to a first embodiment of the present invention, a surface of the path and container which contacts the fluid is made of a thermoplastic resin or rubber material, and the predetermined compound is mixed therein.

The thermoplastic resin is exemplified by polyvinyl chloride, polypropylene, polymethylpentene, polyethylene, an ethylene-vinyl acetate copolymer, polystyrene, acrylonitrile-butadiene-styrene (ABS), polyacrylonitrile, polymethylmethacrylate (PMMA), polyurethane, and elastomers.

The rubber material is exemplified by silicone rubber, butyl rubber, nitrile rubber, isoprene rubber, styrene-butadiene rubber (SBR), and natural rubber.

The thermoplastic resin or rubber material is mixed with a predetermined compoundd (antimicrobial agent) selected from the group consiisting of N-(fluorodichloro-methylthio)-phthalimide, 2-(44-thiazolyl)-benzimidazole, N,N-dimethyl-N'-phenyl-(N-fluuorodichloromethylthio)-sulphamide, 2,4,5,6-tetrachlooroisophthalonitrile, parachlorometaxylenol, sodiumm 2-pyridinethiol-1-oxide, zinc 2-pyridinethiol-1-oxide,, 2,4,4'-trichloro-2'-hydroxydiphenyl ether, and a mixture thereof. Most preferred compounds are N-(flluorodichloromethylthio)-phthalimide, 2-(4-thiazolyl)--benzimidazole, N,N-di-methyl-N'-phenyl-(N-fluorodicbhloromethylthio)-sulphamide, 2,4,5,6-tetrachloroisophthaloonitrile, 2,4,4'-trichloro-2'-hydroxydiphenyl ether, andd a mixture of two or more of these compounds.

The compound elutes fromm the compound-containing thermoplastic resin or rubberr material to be present on the surface and is brought inhto contact with and kills microorganisms existing in thne fluid or reduce the microoganisms to 10^6/mℓ.

The content of the compoound is preferably 1×10^{-4}% to 10% of the thermoplastic reesin (containing a plasticizer, a stabilizer, a lubricant, a pigment, and so on) or the rubber material (ccontaining a filler, a cross-linking agent, a stabiliizer, a pigment, and so on). More specifically, in reespiratory circuits, anesthetic circuits, endotracheal tubes, tracheal

incision tubes, masks, oesopphagus catheters, and drain catheters through which a flluid entering the patient passes, the content of the ccompound is preferably 1×10^{-4}% to 1.0%. Furthermmore, the content of the compound is preferably 1×110^{-3}% to 10% for a medical instrument through which a ffluid passes to flow out of the patient, such as urinaryy catheters and urine bags which are used at the urethrra and catheters used for wounds.

When the content of thee compound is 1×10^{-4}% or more, the present invention provides a better effect.

In a medical instrumentt through which a fluid passes to enter a patient's body, when the content of the compound exceeds 1.0%, tthe content of compound mixed in with the fluid is increassed, and the patient's health may be adversely affected.

In a medical instrumentt through which a fluid passes to flow out of a patiient's body, the compound will be mixed with the fluicd, thereby not affecting the patient. However, the upper limit of the compound content is preferably 10% sGo that the compound does not adversely affect the patienht even when the fluid is flowed in the reverse directtion for some reason.

The composition contaiining the compound can be used to constitute part or all oof the fluid contact surface of the fluid path and contaainer in the medical instru-

A predetermined amount of the selected compound is mixed in with the thermopplastic resin or rubber material, and the resultant mixture can be kneaded well and molded to constitute a mmedical instrument body. When kneading is performed, the compound can often precipitate onto the fluid ccontact surface of the molded body.

For example, as shown iin Figs. 1 and 2, respiratory circuit 11 including flexiblle tube 12, Y connector 13, L connector 14 and endotracheaal tube 16 can be manufactured using a composition off the thermoplastic resin or rubber material which conntains the above-mentioned compound.

As shown in Fig. 3, cloosed urine guide bag 20 including urine guide tube 222, intravenous drip infusion chamber 23, bag body 21, draain tube 25 and connector 26 can be manufactured using thne compcsition of the thermoplastic resin or rubber mateerial which contains one or more of the abcve-mentioned compounds.

Alternatively, the compoound can be mixed in with the thermoplastic resin or rrubber material, and the mixture can be kneaded and formmed into a sheet or pellets. The sheet or pellets is locaated in the surface of the flow path or container in a medical instrument and is brought into contact with a fluid, thereby constituting another medical instrumeent of the present invention.

invention includes a sheet: or pellets which is or are prepared separately. A sheeet or the like must have an overall size small enough for insertion in a bag and must have a thickness of 5 mm or less.

The latter structure is utilized in, especially, a fluid container in a medical instrument such as a urine bag which contains a fluid exhausted from a patient's body.

According to still anoother embodiment, a coating material containing a predetermined amount of the compound can be applied to thee inner surfaces of members constituting a medical instrument of the present invention.

The coating material is exemplified by an organic solvent, a solution type cooating agent, an emulsion or latex type coating agent, aand a hot melt coating agent.

A coating technique iss exemplified by various known techniques such as dip coatting, air knife coating, or spraying.

According to still anoother embodiment, a thermoplastic resin or rubber matterial containing a predetermined amount of a compound described above, and another thermoplastic resin or rubbber material without the compound are used to form aa sheet or tube laminate. The sheet or tube laminate is used for a medical instrument. A layer of thee material containing the compound is formed at the inner side of the tube or bag

and preferably has a thicknness of 1 µm to 500 µm.

In operation of an arttificial respiration circuit 11 in Fig. 1, a pressure iss applied from an artificial respirator (not shown) throough a heater/humidifier (not shown) via flexible tube 122 to guide inspiration air to L connector 14 through Y coonnector 13. The air is then guided from slip joint 15 tto endotracheal tube 16. The air is finally supplied to patient 18.

Expired air opens an eexpired air valve (not shown) and is exhausted from the ppatient's body to tube 16 due to the compliance of patiennt's lungs. The air then passes through joint 15 (inn this case, the inspired air valve is closed) and is exhhausted from connector 14. The air is finally exhausteed from tube 12 through connector 13.

When tube 12 in the reespiration circuit is constituted using members obtaineed by mixing the predetermined ccmpound in with a thermopllastic resin or rubber and kneading and molding the reesultant mixture (Fig. 2), or when a coating material conntaining such a compound is coated on the inner suface or inner and outer surfaces of the members constitutingg the respiration circuit, good sterilization and moldd resistance effects are obtained, and continuous usse can be allowed.

In the bag shown in Fiig. 3, bag body 21, tube 22, chamber 23, tube 25 and connnector 26 are constituted by

the inner surfaces of thesee members are coated with the compound-containing coatingg material, thereby obtaining the similar sterilization eeffect to in respiration circuit 11.

The medical instrumentt according to the present invention is not limited too the cases described above, but can also be applied to anesthetic circuits, endotracheal tubes, tracheal inncision tubes, and masks.

In addition, the medicaal instrument can also be used for catheters used in urine paths and wounds (i.e., urine catheters, drain cathaeters, and oesophagus catheters.

The medical instrument according to the present invention has a fluid contacct surface containing a predetermined compound in thhe fluid path or container. Even if the medical instrumeent is used to constitute an artificial respirator or a cclosed urine guide bag which is used for a long period off time, microorganisms can be decontaminated, thereby prevventing infection.

The present invention aalso prevents cross infection caused by mishandling of thee medical instruments by the medical staff.

In order to prevent dannger of infection, conventional medical instruments mmust be frequently replaced with new ones. However, acccording to the present invention, such frequent replacemment is not necessary, so

to decrease medical cost.

Furthermore, special devices and manipulations are not required to providde the sterilization and mold resistance effects. Therefore, the medical instrument of the present invention ccan be easily used.

The compound-containiing thermoplastic resin or rubber material can be useed as the base, coating or laminate material to constiitute medical instrument bodies. The medical instrcument can be easily manufactured at low cost.

In order to clarify thhe effects of the present invention, a sensitivity diisk method is adapted to measure antibacterial specttra using samples obtained by mixing a compound with a thhermoplastic resin or rubber material. Test results aree shown in Tables 1, 2, 3 and 4.

An antibacterial test is performed by allowing the compound to elute from the thermoplastic resin or rubber material, and test results are shown in Table 5.

1) Sample strains useed in antibacterial spectra according to the sensitivitty disk method are as follows:

Enterobacteriaceae

Klebsiella pneumooniae	IID 875
Escherichia coli	ATCC 25922
Enterobacter cloaacae	IAM 1624
Serratia marcesceens	IID 620

Gram-Negative Anaerobicc Rods

Pseudomonas aeruginosa	ATCC 1001
Acinetobacter anittratus	IID 876
Flavobacterium menningosepticum	ATCC 13253

Gram-Positive Cocci

Staphylococccus aumreus	ATCC 6538P
Streptococcus pneeumoniae	IID 553
Hemophilus influennza	clinical strain

Eumycetes

Candida albicans	Yu 1200
Cryptococcus neofformans	IAM 12253
Aspergillus fumiggatus	IAM 2004

The test was perfoimed in the following manner.

Preparation of Samples

Sheets (about 1 mm thicck) of ethylene-vinylacetate (EVA) copolymer (vinylacetaate content: 10%) containing N-(fluorodichlorometnylthio)-phthalimide, 2-(4-thiazolyl)-benzimidazole, NN,N-dimethyl-N'-phenyl-(N-fluorodichloromethylthio)-ssulphamide, 2,4,5,6,-tetrachloroisophthalonitrile at contents of 0.2, 0.4, 0.8, 1.5, and 3.0% were prepared, and samples having a diameter of 10 mm (0.79 cm^2) were punched.

The samples were steriilized.

Sterilization was perfformed in accordance with the EOG sterilization method, aand the sterilized samples

one week and were degassed..

The test method is desscribed by Nobuo Tanaka, Outline Of Antibiotics, 2ndd ed., Tokyo University Press, 1977, as follows.

Sensitivity measuring culture media were prepared.

Heart Infusion Agar (DDIFCO): HIA was used for bacteria, and Sabouraud Gluucose Agar (Eiken): SGA was used for eumycetes. The cuulture media for the respective bacteria in an amount of 20 mℓ each were poured in petri dishes having a diameeter of 90 mm and were dried for 20 minutes in a germ-frree state.

Starters were then preepared.

Bacteria were inoculatted in Heart Infusion Broth (DIFCO) and were cultured aand proliferated at a temperature of 37°C for 15 to 20 hours. Sabouraud Glucose Agar was directly suspendedd in distilled water. The culture media were thus preepared to a concentration of about 10^8/mℓ each.

The bacteria liquids wwere inoculated in the culture media.

As shown in Fig. 4, 4 mℓ of agar culture medium 63 (HIA, SAG) adced with each starter was uniformly poured on sensitivity measuring cuulture medium 61 and was solidified.

The number of bacteriaa inoculated was about 6.4×10^5 to 6.4×10^6 per plate. When the agar was

a germ-free state. As shhown in Fig. 4, samples 65 were placed on medium 63 and ccultured at a temperature of 31°C for 24 hours. Eumyccetes were cultured for about 48 hours.

The results were evaaluated such that (minor axis + major axis)/2 was calculaated as a diameter of an inhibition circle and are shownn in Tables 1, 2, 3 and 4. The diameter was measured in units of cm, and mark "-" indicates that no inhibittion circuit is found.

Table 1

Inhibition Circle Observed for Each Strain — Preventol A-3

N-(fluorodichlorommethylthio)-phthalimide

Strain \ Concentration	0.2 %%	0.4	0.8	1.5	3.0
Kl. pneumonial	-**	-	1.05	1.1	1.1
E. coli	1.05	1.1	1.2	1.2	1.2
B. aeruginosa	-	-	-	1.05	1.05
Aci. anitratus	1.25	1.25	1.25	1.3	1.3
S. aureus	1.4	1.45	1.55	1.55	1.55
Str. pneumonial	1.4	1.4	1.5	1.5	1.5
H. influenza	1.8	1.65	1.7	1.75	1.75
C abbicans	3.6	3.6	3.3	3.3	3.35
Cr. neoformans	6	5.25	5.55	5.8	5.55
As. fumigatus	1.95	1.85	1.25	2.3	2.1
En. cloacal	1.05	1.05	1.1	1.15	1.2
Ser. marcescens	1.1	1.15	1.2	1.25	1.25
P. vulgaris	1.2	1.2	1.25	1.25	1.25
F. memingo-septicum	1.5	1.5	1.6	1.55	1.6

Unit (cm) * No inhibition circle observed

Tabble 2

TBZ (Hokster HP) 2-(44-thiazolyl)-benzimidazole

Concentration / Strain	0.2 %	0.4	0.8	1.5	3.0
Kl. pneumonial	-	-	-	-	-
E. coli	-	-	-	-	-
B. aeruginosa	-	-	-	-	-
Aci. anitratus	-	-	-	-	-
S. aureus	-	-	-	-	-
Str. pneumonial	-	-	-	-	-
H. influenza	-	-	-	-	-
C abbicans	1.45	-	1.35	1.05	1.90
Cr. neoformans	1.85	1.60	1.95	1.85	2.40
As. fumigatus	-	-	-	-	-
En. cloacal	-	-	-	-	-
Ser. marcescens	-	-	-	-	-
P. vulgaris	-	-	-	-	-
F. memingo-septicum	-	-	-	-	-

In columns with no numeerals, no innibition circle was observed.

Tabble 3

Preventol A-4 N,N-diimethyl-N'-phenyl(N-fluorodichlorommethylthio)-sulphamide

Concentration / Strain	0.2 %	0.4	0.8	1.5	3.0
Kl. pneumonial	--	-	-	-	-
E. coli	--	-	-	-	-
B. aeruginosa	--	-	-	-	-
Aci. anitratus	1.05	1.10	1.10	1.10	1.10
S. aureus	1.15	1.30	1.25	1.30	..30
Str. pneumonial	1.40	1.50	1.45	1.40	1.50
H. influenza	1.60	1.55	1.50	1.55	1.55
C abbicans	2.90	3.30	2.80	2.85	3.0
Cr. neoformans	5.30	5.75	5.10	5.25	5.35
As. fumigatus	2.05	2.70	2.35	2.35	2.30
En. cloacal	-	-	-	-	1.05
Ser. marcescens	-	-	-	1.15	1.15
P. vulgaris	-	-	-	-	-
F. memingo-septicum	1.15	1.20	1.20	1.30	1.20

Tablle 4

Nobcocide N-96 2,4,5,6-tettrachloroisophthalonitrile

Concentration / Strain	0.2 %%	0.4	0.8	1.5	3.0
Kl. pneumonial	-	-	-	-	-
E. coli	-	-	-	-	-
B. aeruginosa	-	-	-	-	-
Aci. anitratus	-	-	-	-	-
S. aureus	1.05	1.25	1.25	1.25	1.30
Str. pneumonial	-	-	-	-	-
H. influenza	1.20	1.30	1.40	1.45	1.40
C abbicans	1.05	1.15	1.15	1.20	1.20
Cr. neoformans	2.85	3.05	3.50	3.40	3.45
As. fumigatus	-	-	-	-	1.1
En. cloacal	-	-	-	-	-
Ser. marcescens	-	-	-	-	-
P. vulgaris	-	-	-	-	-
F. memingo-septicum	-	1.05	1.10	1.15	1.15

2) Antibacterial testt strains used for determining the effect of a microbial agent eluted from a sample were as follows.

Escherichia coli	ATCC 25922
Staphylococcus aureus	ATCC 6538p

The samples were prepaared as follows.

EVA copolymers containning 0.001%, 0.0025%, 0.01% and 0.02% of N-(fluorodichlloromethylthio)-phthalimide (Preventol A-3) were preparred, and samples were punched therefrom. Each sample has a diameter of 1 cm (0.79 cm^2).

The test was performedd as follows.

Five samples were dippoed in 1.5 mℓ of distilled water, and an extraction raate is set to be 0.19 mℓ/cm^2. The samples were left to steand at a temperature of 31°C for 17 hours, and inoculatiion was performed such that the concentration is set to be 10^6/mℓ. The number of live bacteria was measured aafter 1, 4, 7 and 24 hours as well as after 1, 3, 6 and 244 hours. The number of live bacteria is given as a logarrithmic value. The results are shown in Table 5.

Tablle 5

Compound Concentration annd Antibacterial Property

(Numerals are Logarithmic Values of Live Bacteria After the Test)

Strain / Time / Con-centration	E. coli			
	1 hr	4 hr	7 hr	24 hr
0.001 %	6.31	6.51	6.63	6.28
0.0025	6.48	6.70	6.69	6.20
0.005	6.54	6.64	6.61	6.04
0.01	6.56	6.64	6.57	2 >
0.02	6.30	6.26	6.30	2 >
Blank	6.64	6.51	6.76	6.57

Strain / Time / Con-centration	S. aureus			
	1 hr	33 hr	6 hr	24 hr
0.001 %	6.30	55.99	5.93	3.78
0.0025	6.04	66.04	5.94	4.36
0.005	6.34	66.26	5.91	3.89
0.01	6.18	66.45	6	2.49
0.02	5.88	55.60	5.08	0
Blank	6.89	66.18	5.92	4.11

The effects of the preseent invention are apparent

As described above, thne antimicrobial agent used in the present invention exhibits an antimicrobial effect over a long period of time,, as compared to the prior art antimicrobial agent. Furthner, when the antimicrobial agent is mixed in with a material forming the main body of the instrument according to the present invention, the antimicrobial agent contained in the material elutes on the surface of the main body during storage or the like, resulting in obtainingg superior antimicrobial effect produced during usage without cumbersome operation such as coating. The claimss form part of the disclosure.

The claims defining thhe invention are as follows:

1. A medical instrrument having a fluid path or container wherein the instrrument comprises:

a main body of the meddical instrument; and

at least one antimicroobial agent located on at least a surface of the fluid path oof the main body and selected from the group consisting of NN-(fluorodichloromethylthio)-phthalimide, 2-(4-thiazolyll)-benzimidazole, N,N-dimethyl-N'-phenyl-(N-fluorodichlorommethylthio)-sulphamide, 2,4,5,6-tetrachloroisophtharonitrille, parachlorometaxylenol, sodium 2-pyridinethiol-1-oxide, ziinc 2-pyridinethiol-1-oxide, and 2,4,4'-trichloro-2'hydroxyphhenyl ether, wherein the agent is at an effective levell such that the increase of microorganisms contacting tthe surface is suppressed.

2. An instrument acccording to claim 1, wherein said main body is entirely forrmed of a thermoplastic resin or rubber composition containiing said antimicrobial agent.

3. An instrument acccording to laim 2, wherein the composition contains 1 x 10^{-4} wt% to 10 wt% of said antimicrobial agent.

4. An instrument acccording to claim 1, wherein said surface is covered with a coating material containing said antimicrobial agent.

5. An instrument acccording to claim 4, wherein the coating agent contains 11 x 10^{-4} wt% to 10 wt% of said antimicrobial agent.

6. A medical innstrument, substantially as hereinbefore described withh reference to Figs. 1 to 3 of the accompanying drawings.

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FIG. 3

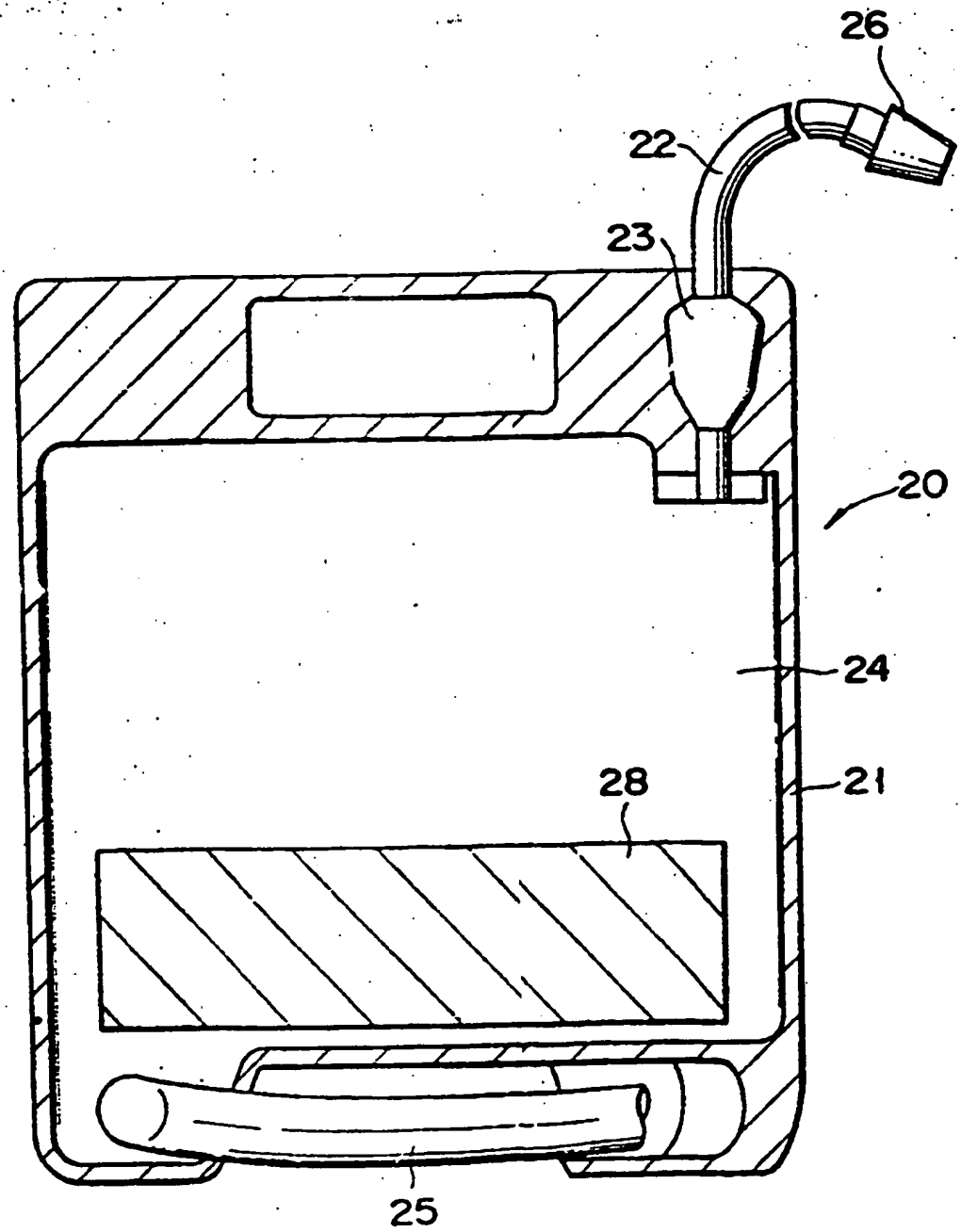

FIG. 4